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ART UNIT	PAPER NUMBER
1647	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/622,313	BARDEN ET AL.	
	Examiner	Art Unit	
	Jon M. Lockard	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 September 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-72* is/are pending in the application.

4a) Of the above claim(s) *10,15-31,41,43-49,51-54 and 65-71* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9,11-14,32-40,42,50,55-64 and 72* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-72* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *17 July 2003* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/24/06, 7/25/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group II, claims 1-9, 11-15, 17, 32-40, 42-43, 50, 55-59, 60-64, and newly added claim 72, in so far as they are drawn to antibodies adapted to distinguish between functional $P2X_7$ receptors and non-functional $P2X_7$ receptors, wherein the antibodies bind an epitope extending from Gly200 to Cys216 of the $P2X_7$ receptors (and compositions and kits comprising the same), in the reply filed 07 September 2006 is acknowledged. With regards to the election of species requirement set forth at pg 14-15 of the previous Office Action (mailed 16 June 2006), Applicant's election without traverse of skin cancer as the type of disease/condition in the reply filed on 07 September 2006 is acknowledged. Accordingly, claims 15, 17, and 43 are withdrawn from further consideration as being drawn to a nonelected species.

2. Therefore, claims 10, 15-31, 41, 43-49, 51-54, and 65-71 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 07 September 2006.

3. The restriction requirement is still deemed proper and is therefore made **FINAL**.

Status of Application, Amendments, And/Or Claims

4. The Response to the Restriction Requirement filed on 07 September 2006 has been entered in full. Claims 17, 27, 32, 37, 52, 55, 57-59, and 62 have been amended, claims 10, 15-31, 41, 43-49, 51-54, and 65-71 have been withdrawn from further consideration as discussed

above, and claim 72 has been added. Therefore, claims 1-72 are pending and claims 1-9, 11-14, 32-40, 42, 50, 55-64, and 72 as they read upon the elected invention set forth above, are the subject of this Office Action.

Information Disclosure Statement

5. The information disclosure statement (IDS) submitted on 25 July 2006 has been considered by the examiner. The information disclosure statement filed 24 May 2006 fails to comply with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609 because copies of references AB-AJ have not been provided. It has been placed in the application file, but the information referred to therein (references AB-AJ) has not been considered as to the merits. Applicant is advised that the date of any re-submission of any item of information contained in this information disclosure statement or the submission of any missing element(s) will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the statement, including all certification requirements for statements under 37 CFR 1.97(e). See MPEP § 609.05(a).

6. Applicant states that copies of the references should have been provided to the USPTO pursuant to the sharing agreement between WIPO and the USPTO since the subject application is a US national phase of international application PCT/AU02/0061. However, it is noted that the instant application is a CIP of PCT/AU02/0061 as indicated on the application data sheet (ADS) filed 17 July 2003. Moreover, since the instant application has not been processed as a national stage entry, copies of the domestic priority documents (PCT/AU02/0061 and PCT/AU02/01204) and the foreign priority documents (PR2579, PR5890, PR5891, PR7430, and PR7431) have not been received by the USPTO.

Drawings

7. The drawings are objected to because the figure in the instant application does not comply with 37 C.F.R. 1.84(U)(1), which states that "[w]here only a single view is used in an application to illustrate the claimed invention, it must not be numbered and the abbreviation "FIG" must not appear".

8. Figure 1 should be designated by a legend such as --Prior Art-- because only that which is old is illustrated (See pg 16[0074] of the Specification). See MPEP § 608.02(g). Corrected drawings in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. The replacement sheet(s) should be labeled "Replacement Sheet" in the page header (as per 37 CFR 1.121(d)) so as not to obstruct any portion of the drawing figures. If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

9. Applicants are advised that upon issuance of a patent, the complete text of the sequence listing submitted in compliance with 37 C.F.R.§§1.821-1.825 will be published as part of the patent. Therefore, it is unnecessarily redundant to repeat the sequence information in the form of Figures. It is therefore noted that Applicants may overcome the objections to the drawing set forth above by amending the specification to delete any Figures (e.g. Figure 1) which consist only of nucleic acid or protein sequences which have been submitted in their entirety in computer readable format (i.e. as SEQ ID NO:'s), in which case they should further amend the specification accordingly to reflect the replacement of the Figure by the appropriate SEQ ID NO.

Specification

10. The disclosure is objected to because of the following informalities:

11. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The following title is suggested: "Antibodies to non-functional $P2X_7$ receptor".

12. The use of the trademarks has been noted in the Specification (See pg 19[0095], pg 20[0096], and pg 25[0125], for example). Trademarks should be capitalized wherever they appear and should be accompanied by the generic terminology. Applicant is encouraged to review and make appropriate corrections to the specification regarding the misuse of trademarks. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner that might adversely affect their validity as trademarks. Appropriate correction is suggested.

13. The abstract of the disclosure is objected to because it is more than one paragraph in length. See MPEP § 608.01(b). Applicant is reminded of the proper language and format for an abstract of the disclosure. The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 150 words. It is important that the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the printer is limited. The form and legal phraseology often used in patent claims, such as "means" and "said," should be avoided. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details. The language should be clear and concise and should not repeat information given in

the title. It should avoid using phrases which can be implied, such as, "The disclosure concerns," "The disclosure defined by this invention," "The disclosure describes," etc. Appropriate correction is suggested.

Claim Objections

14. Claim 6 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. In the instant case the recitation of "natural or artificial" does not further limit the probe of claim 1, since natural or artificial are the only two possibilities.

15. Claims 11, 12, 14, 42, and 50 are objected to because of the following informalities: Claims 11, 12, 14, 42, and 50 encompass non-elected inventions, e.g., "wherein the probe is or *includes* an antibody" (claims 11 and 12); prostate, breast, lung, cervix, uterus, stomach, oesophagus, bladder, colon, and vaginal cancers, other epithelial cell cancers, malignant lymphoma, other blood cancers, irritable bowel syndrome, and infection by a virus or other pathological organism (claims 14 and 42); and "an epitope to cause the generation of such an amount" (claim 50). Appropriate correction is suggested.

16. Although not indefinite, the Examiner requests for the purpose of clarity that the phrase "when the scanning technology is positron emission tomography" in claim 57 be replaced with the following: "wherein the scanning technology is positron emission tomography". Appropriate correction is suggested.

17. In claim 64, line 1, the phrase "a probe that that" should be amended to recite "a probe that". Appropriate correction is suggested.

Claim Rejections - 35 USC § 101

18. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

19. Claims 7-8, 11-13, 32-40, 42, and 55 are rejected under 35 U.S.C. § 101 because the claimed invention is directed to non-statutory subject matter. The claims read on a product of nature in that the claimed antibody is not "isolated". The claims encompass, for example, an antibody that has not been removed from the human or animal. In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. See *Diamond v. Chakrabarty*, 447 U.S. 303, 206 USPQ 193 (1980). The claims should be amended to indicate the hand of the inventor, e.g., by insertion of "isolated" or "purified". See MPEP 2105.

Claim Rejections - 35 USC § 112, 2nd Paragraph

20. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

21. Claims 1-9, 11-14, 32-40, 42, 50, 55-64, and 72 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

22. Claims 1-4, 9, 32-35, 38, 63, and 72 are rejected as being indefinite because it is unclear what is meant by the phrase "adapted to distinguish/detect". Because neither the claims nor the specification identify how the probe or antibody is adapted, the metes and bounds of the claims cannot be determined.

23. Claims 1-5, 9, 11-13, 32-36, 38-40, 50, 60-64, and 72 are rejected as being indefinite because they recite $P2X_7$. The mere recitation of a name, i.e., $P2X_7$, is insufficient to indicate the metes and bounds of the claims as the term was not well-established in the art at the time the invention was filed. It is suggested that the term be identified by sufficient structural and/or functional language (i.e., SEQ ID NO:) to overcome this rejection.

24. Claims 7, 37, and 55 are rejected as being indefinite because it is unclear if the limitation "a fragment thereof" refers to a fragment of the polyclonal antibody, a fragment of the monoclonal antibody, a fragment of the recombinant antibody, a fragment of the humanized antibody, a fragment of the human antibody, or if it refers to a fragment of any of the previously mentioned antibodies. Therefore, the metes and bounds of the claims cannot be determined. Additionally, it is unclear what is meant by the recitation of "an appropriate fragment" in claim 37. Does it refer to the size of the fragment, the binding properties of the fragment, or something completely different? Without knowing what would make a fragment "appropriate", the metes and bounds of the claims cannot be determined.

25. Claim 8 recites the limitation "an epitope of each receptor in an extracellular domain adjacent to a site for binding ATP" in line 2 of the claim. There is insufficient antecedent basis for this limitation in the claim.

26. Claims 9, 11-13, 38-40, 64, and 72 are rejected as being indefinite because they recite certain amino acid positions. However, no reference sequences are defined in the claims. Given the variations of published sequences contained in the databases, it is unclear which amino acid positions are encompassed by the claims. Moreover, numbering is not an inherent property of a nucleic acid or protein sequence. Accordingly, recitation of a number without reference to a specific sequence is indefinite.

27. A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claims 11 and 12 recite the broad recitation “wherein the probe includes an antibody”, and the claims also recite “wherein the probe is an antibody”, which is the narrower statement of the range/limitation.

28. Claims 11-12 are rejected as being indefinite because it is unclear what is meant by the phrase “wherein the probe is or includes an antibody”. For example, does it refer to a

composition comprising a probe and an antibody, or does it refer to a probe conjugated to an antibody?

29. Claim 50 is indefinite for reciting the phrase "aberrant or non-functional $P2X_7$ receptors". Since neither the Specification nor the art defines "aberrant" $P2X_7$ receptors unambiguously, the metes and bounds of the claim cannot be determined.

30. Claims 56, 58, and 59 are rejected as being indefinite because it is unclear what is meant by the phrase "when combined with". Does it refer to an antibody with a radiolabel attached thereto, does it refer to a combination comprising an antibody and a radiolabel, or does it refer to a method?

31. Claims 60-62 are rejected as being indefinite because it is unclear what is meant by the phrase "together with a normal $P2X_7$ receptor expression profile". Since neither the Specification nor the art defines a "normal $P2X_7$ receptor expression profile" unambiguously, the metes and bounds of the claims cannot be determined.

32. Claims 6, 14, 42, and 57 are rejected for depending from an indefinite claim.

Claim Rejections - 35 USC § 112, 1st Paragraph (Scope of Enablement)

33. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

34. Claims 1-9, 11-14, 32-40, 42, 50, 55-64, and 72 are rejected under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for:

(1) an isolated antibody that specifically binds to residues G200-C216 of SEQ ID NO:1, as well as compositions comprising the same and a pharmaceutically acceptable carrier;

(2) an isolated antibody that specifically binds to residues G200-T215 of SEQ ID NO:1, as well as compositions comprising the same and a pharmaceutically acceptable carrier;

(3) a probe for detection of non-functional $P2X_7$ receptors, wherein the probe is selected from the group consisting of (a) an isolated antibody that specifically binds to residues G200-C216 of SEQ ID NO:1, and (b) an isolated antibody that specifically binds to residues G200-T215 of SEQ ID NO:1; and

(4) a kit comprising an antibody that specifically binds to an epitope within residues G200-C216 of the $P2X_7$ receptor of SEQ ID NO:1 without specifically binding to other regions of the $P2X_7$ receptor, and an antibody that specifically binds to an epitope within residues V65-K81 of the $P2X_7$ receptor of SEQ ID NO:1 without specifically binding to an epitope within residues G200-C216 of the $P2X_7$ receptor of SEQ ID NO:1,

does not reasonably provide enablement for the following: a "probe" or antibody for detection of *a* disease or condition, wherein

(1) the probe or antibody is adapted to distinguish between functional P2X7 receptors and non-functional receptors and kits comprising the same;

(2) the probe or antibody is adapted to distinguish between functional $P2X_7$ receptors and non-functional receptors by detecting a change in binding of one or more proteins necessary for pore formation in $P2X_7$ receptors;

(3) wherein the probe or antibody is adapted to distinguish between functional $P2X_7$ receptors and non-functional receptors by detecting one or more parts of the receptor exposed in the absence of bound ATP;

(4) wherein the probe is an antibody chosen from the group consisting of a polyclonal antibody, a monoclonal antibody, a recombinant antibody, a humanized antibody, a human antibody and a fragment thereof;

(5) the probe is an antibody directed against an epitope of each receptor located in an extracellular domain adjacent to a site for binding ATP;

(6) the probe or antibody is adapted to distinguish between functional receptors having a sequence in which proline at amino acid 210 is in the trans conformation and non-functional receptors having a sequence in which the proline at amino acid 210 is in the cis conformation;

(7) the antibody is adapted to distinguish between functional $P2X_7$ receptors and non-functional $P2X_7$ receptors and to bind only non-functional receptors and kits comprising the same;

(8) the antibody is adapted to distinguish between functional $P2X_7$ receptors and non-functional $P2X_7$ receptors by detecting change in relation to binding of adenosine triphosphate (ATP) to the receptors;

(9) a pharmaceutical composition for treatment or prevention of a disease or condition in a patient, the composition including a pharmaceutically effective amount of an antibody being adapted to distinguish between functional $P2X_7$ receptors and non-functional $P2X_7$ receptors and to bind only non-functional receptors, capable of regulating programmed cell death of cells having expressed on their surface aberrant or non-functional $P2X_7$ receptors; or

(10) a diagnostic kit comprising a probe that specifically binds to an epitope within residues Gly200 to Cys216 of a $P2X_7$ receptor without specifically binding to other regions of the $P2X_7$ receptor, and a probe that specifically binds an epitope outside residues Gly200 to Cys216 of a $P2X_7$ receptor without specifically binding to an epitope Gly200 to Cys216 of the $P2X_7$ receptor.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

35. The specification's disclosure is insufficient to enable one skilled in the art to practice the invention as broadly claimed without undue experimentation. The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

36. The claims are drawn very broadly to a "probe" or antibody for detection of *a* disease or condition, wherein (1) the probe or antibody is adapted to distinguish between functional $P2X_7$ receptors and non-functional receptors and kits comprising the same, (2) the probe or antibody is adapted to distinguish between functional $P2X_7$ receptors and non-functional receptors by detecting a change in binding of one or more proteins necessary for pore formation in $P2X_7$ receptors, (3) wherein the probe or antibody is adapted to distinguish between functional $P2X_7$ receptors and non-functional receptors by detecting one or more parts of the receptor exposed in the absence of bound ATP, (4) wherein the probe is an antibody chosen from the group consisting of a polyclonal antibody, a monoclonal antibody, a recombinant antibody, a humanized antibody, a human antibody and a fragment thereof, (5) the probe is an antibody directed against an epitope of each receptor located in an extracellular domain adjacent to a site for binding ATP, (6) the probe or antibody is adapted to distinguish between functional receptors having a sequence in which proline at amino acid 210 is in the trans conformation and non-

functional receptors having a sequence in which the proline at amino acid 210 is in the cis conformation, (7) the antibody is adapted to distinguish between functional $P2X_7$ receptors and non-functional $P2X_7$ receptors and to bind only non-functional receptors and kits comprising the same, (8) the antibody is adapted to distinguish between functional $P2X_7$ receptors and non-functional $P2X_7$ receptors by detecting change in relation to binding of adenosine triphosphate (ATP) to the receptors, (9) a pharmaceutical composition for treatment or prevention of a disease or condition in a patient, the composition including a pharmaceutically effective amount of an antibody being adapted to distinguish between functional $P2X_7$ receptors and non-functional $P2X_7$ receptors and to bind only non-functional receptors, capable of regulating programmed cell death of cells having expressed on their surface aberrant or non-functional $P2X_7$ receptors, or (10) a diagnostic kit comprising a probe that specifically binds to an epitope within residues Gly200 to Cys216 of a $P2X_7$ receptor without specifically binding to other regions of the $P2X_7$ receptor, and a probe that specifically binds an epitope outside residues Gly200 to Cys216 of a $P2X_7$ receptor without specifically binding to an epitope Gly200 to Cys216 of the $P2X_7$ receptor.

37. While the specification discloses an isolated antibody that specifically binds to residues G200-C216 of SEQ ID NO:1, wherein the antibody distinguishes between functional and non-functional receptors by binding non-functional $P2X_7$ receptors without binding to functional P2X7 receptors (See Example 4), the specification fails to describe other probes, which the specification discloses may be natural and artificial and may include polypeptides, beta-turn mimetics, polysaccharides, phospholipids, hormones, prostaglandins, steroids, aromatic compounds, heterocyclic compounds, benzodiazepines, oligomeric N-substituted glycines and

oligocarbamates (See pg 4[0013]), or antibodies which are capable of distinguishing between functional and non-functional $P2X_7$ receptors. While the specification teaches that the epitope within residues G200-C216 of SEQ ID NO:1 is adjacent to the ATP binding site and undergoes a conformational change (proline at position 210 of SEQ ID NO:1 is in the cis conformation) in the absence of bound ATP (See for example pg 20-21[0098]-[0099]), the specification does not provide working examples of, or any guidance on how to make the following:

(1) any *probe* that specifically binds an epitope within residues G200-C216;

(2) any probe or antibody that detects a change in binding of one or more proteins necessary for pore formation in $P2X_7$ receptors;

(3) any probe or antibody that detects one or more parts of the receptor exposed in the absence of bound ATP;

(4) any probe or antibody that directed against other epitopes located in an extracellular domain adjacent to a site for binding ATP;

(5) any probe or antibody that is adapted to distinguish between functional receptors having a sequence in which proline at amino acid 210 is in the trans conformation and non-functional receptors having a sequence in which the praline at amino acid 210 is in the cis conformation; or (6) any probe or antibody that detects a change in relation to binding of ATP, other than the antibody that specifically binds to residues G200-C216 of SEQ ID NO:1 and the antibody that specifically binds to residues G200-T215 of SEQ ID NO:1.

Moreover, the disclosure has not shown (1) other proteins necessary for pore formation in $P2X_7$ receptors or how they could be detected; (2) with the exception of a proline at amino acid 210 of SEQ ID NO:1, other parts of the receptor exposed in the absence of bound ATP; (3) other epitopes located in an extracellular domain adjacent to a site for binding ATP.

38. Furthermore, claim 50 is drawn to a pharmaceutical composition for treatment or prevention of a disease or condition in a patient. However, other than the *treatment* of skin cancer (See pg 22[0104] and pg 25[0124]), the specification as filed does not provide adequate guidance on how to treat or prevent any disease or condition, nor is it at all predictable that a pharmaceutical composition comprising an antibody that binds only non-functional P2X7 receptors could be used to treat or prevent any disease or condition. With regards to this portion of the rejection, amendment of the claim to recite, for example, "A composition comprising the antibody of claim 32 and a pharmaceutically acceptable carrier" would be remedial.

39. Due to the large quantity of experimentation necessary to generate the infinite number of derivatives recited in the claims and possibly screen same for differential binding (i.e., non-functional *vs.* functional), the lack of direction/guidance presented in the specification regarding which structural features are required in order to provide differential binding, the absence of working examples directed to same, the complex nature of the invention, and the breadth of the claims which fail to recite any structural limitations, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Claim Rejections - 35 USC § 112, 1st Paragraph (Written Description)

40. Claims 1-9, 11-14, 32-40, 42, 50, 55-64, and 72 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

41. The claims are drawn very broadly to a "probe" or antibody for detection of *a* disease or condition, wherein (1) the probe or antibody is adapted to distinguish between functional $P2X_7$ receptors and non-functional receptors and kits comprising the same, (2) the probe or antibody is adapted to distinguish between functional $P2X_7$ receptors and non-functional receptors by detecting a change in binding of one or more proteins necessary for pore formation in $P2X_7$ receptors, (3) wherein the probe or antibody is adapted to distinguish between functional $P2X_7$ receptors and non-functional receptors by detecting one or more parts of the receptor exposed in the absence of bound ATP, (4) wherein the probe is an antibody chosen from the group consisting of a polyclonal antibody, a monoclonal antibody, a recombinant antibody, a humanized antibody, a human antibody and a fragment thereof, (5) the probe is an antibody directed against an epitope of each receptor located in an extracellular domain adjacent to a site for binding ATP, (6) the probe or antibody is adapted to distinguish between functional receptors having a sequence in which proline at amino acid 210 is in the trans conformation and non-functional receptors having a sequence in which the proline at amino acid 210 is in the cis conformation, (7) the antibody is adapted to distinguish between functional $P2X_7$ receptors and non-functional $P2X_7$ receptors and to bind only non-functional receptors and kits comprising the same, (8) the antibody is adapted to distinguish between functional $P2X_7$ receptors and non-functional $P2X_7$ receptors by detecting change in relation to binding of adenosine triphosphate (ATP) to the receptors, (9) a pharmaceutical composition for treatment or prevention of a disease or condition in a patient, the composition including a pharmaceutically effective amount of an antibody being adapted to distinguish between functional $P2X_7$ receptors and non-functional

$P2X_7$ receptors and to bind only non-functional receptors, capable of regulating programmed cell death of cells having expressed on their surface aberrant or non-functional $P2X_7$ receptors, or (10) a diagnostic kit comprising a probe that specifically binds to an epitope within residues Gly200 to Cys216 of a $P2X_7$ receptor without specifically binding to other regions of the $P2X_7$ receptor, and a probe that specifically binds an epitope outside residues Gly200 to Cys216 of a $P2X_7$ receptor without specifically binding to an epitope Gly200 to Cys216 of the $P2X_7$ receptor. The claims also recite kits and compositions comprising the polypeptides. The claims do not require that the probe or antibody possess any particular conserved structure or other disclosed distinguishing feature. Thus, the claims are drawn to a genus of polypeptides that are defined only by a desired binding selectivity.

42. To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of compete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claims is a partial function in the form of a recitation of desired binding selectivity. There is not even identification of any particular portion of the structure that must be conserved. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus. Additionally, the description of two antibody species ((1) an isolated antibody that specifically binds to residues G200-C216 of SEQ ID NO:1, and (2) an isolated antibody that specifically

binds to residues G200-T215 of SEQ ID NO:1) is not adequate written description of an entire genus of functionally equivalent probes.

43. *Vas-Cath Inc. v. Mahurkar*, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed"* (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed" (See *Vas-Cath* at page 1116).

44. With the exception of the antibodies referred to above, the skilled artisan cannot envision the detailed chemical structure of the encompassed probes, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The polypeptide itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

45. One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

46. Therefore, only (1) an isolated antibody that specifically binds to residues G200-C216 of SEQ ID NO:1, and (2) an isolated antibody that specifically binds to residues G200-T215 of SEQ ID NO:1, but not the full breadth of the claims meets the written description provision of 35

U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Summary

47. No claim is allowed.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Jon M. Lockard, Ph.D.** whose telephone number is **(571) 272-2717**. The examiner can normally be reached on Monday through Friday, 8:00 AM to 6:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Brenda Brumback**, can be reached on **(571) 272-0961**.

The fax number for the organization where this application or proceeding is assigned is **571-273-8300**.

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November 15, 2006

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